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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,619	10/10/2001	Erin Schuetz	44158/244344	8446

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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,619	SCHUETZ ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-32* is/are rejected.

7)☒ Claim(s) *12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

9-0-0

DETAILED ACTION

1. Currently, claims 1-32 are pending in the instant application. The amendments and arguments filed 7/20/2004, 11/12/2004, and 1/26/2005 have been thoroughly reviewed but are deemed insufficient to place the instant application in condition for allowance. The following rejections are newly applied or reiterated. They represent the complete set being presently applied to the instant office action. Any rejection not reiterated is hereby withdrawn in view of the amendments to the claims. This action is NON-FINAL.

2. The examiner reviewing your application has changed. The new examiner is Jehanne Sitton in art unit 1634. Please direct all future correspondence to the new examiner.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

4. Claims 24 and 25 are objected to because of the following informalities:

Claims 24 and 25 are objected to. Line 3 of each claim contains a number (20 and 25 respectively) that appear to have been inadvertently copied from a previous version of the claim. In previous amendments, these numbers were placed at the margin to designate line numbers of a particular page. Appropriate correction is required.

Specification

5. The disclosure is objected to because the amendments to the specification which refer to SEQ ID NO: 73 of figure 3 or SEQ ID NO: 74 of Figure 5 are confusing. Figures 3 and 5 do not contain SEQ ID NO: 73 or 74 respectively. This objection can be overcome by deleting reference to Figure 3 or 5 in each iteration. Appropriate correction is required.

6. The amendment filed 7/20/2004 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendment to the specification at page 78, replacing the paragraph at line 6 introduces New Matter into the specification. The recitation of "Quantity One" program was changed to 'QUALITY ONE" program. However, the specification as originally filed does not provide support for the QUALITY ONE program. Accordingly, the amendment introduces new matter into the specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

7. Claims 1-7, 16-22 and 26-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-7 are indefinite in the recitation of predicts "a relatively high level of expression" and predicts "a relatively low level of expression". The terms "high" and "low" are

terms of degree and do not make clear any specific value. The additional use of the term "relatively" appears to intend to provide a comparison but the comparison is not made clear in the claim. Accordingly, the metes and bounds of each "wherein" clause in the claims is unclear. This rejection can be overcome by reciting a comparison. For example: "wherein the presence of an A at the position corresponding to nucleotide 23 of SEQ ID NO: 73 on at least one CYP3A5 allele of said subject predicts a relatively higher level of expression of CYP3A5 as compared to the presence of a G at that position...".

B) Claims 16-19 are indefinite over the recitation of "the PCR product" in step (b)(i) of claim 16, and claims 26-29 are indefinite over the recitation of "the PCR product" in step (b)(i) of claim 26 because there is insufficient antecedent basis for this claim. This rejection can be overcome by reciting "the PCR product produced by amplification with the first and second primer".

C) Claims 20-22 are indefinite over the recitation of "the PCR product" in step (c)(i) and claims 30-32 are indefinite over the recitation of "a PCR product" in step (c)(i) because it is unclear which PCR product is being referred to in the claims. The claims are directed to more than one amplification reaction and consequently it is unclear which amplification fragment is being referred to. This rejection can be overcome by using the designator "first" or "second" when reciting a PCR product or amplification fragment, so that they can be distinguished.

D) Claims 14-15, 18-19, 21-22, 24-25, 28-29, and 31-32 are indefinite in the recitation of "primer [X or Y] has the sequence corresponding to SEQ ID NO:" because it is unclear if the primer has the sequence of the SEQ ID NO: or not. While the use of the term "corresponding" is not indefinite in claims with regard to the nucleotide position of a particular SEQ ID NO: where

the claim makes clear that this position is in intron 3 or exon 7 of CYP3A5, the use of such term with regard to the primers is confusing because it is not clear whether the primer has the sequence or not. This rejection can be overcome by reciting instead "wherein primer [X orY] has the sequence of SEQ ID NO:..."

E) Claims 13-32 are indefinite in the recitation of "position corresponding to nucleotide 23 of SEQ ID NO: 73" or "position corresponding to nucleotide 29 of SEQ ID NO: 74" because the claim does not make clear what this position is in reference to. Without some reference point, it is not clear if the claims are intended to be limited to only detecting SEQ ID NO: 73 or SEQ ID NO: 74. Claims 1 and 8 state that such positions are in intron 3 or exon 7, which serves to provide a reference point for SEQ ID NO: 73 or 74 in CYP3A5. However, claims 13, 16, 20, 23, 26, and 30 are silent with respect to such. This rejection can be easily overcome by reciting instead "position corresponding to nucleotide 23 of SEQ ID NO: 73 in intron 3" or "position corresponding to nucleotide 29 of SEQ ID NO: 74 in exon 7".

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claims 1, 2, and 5 are rejected under 35 U.S.C. 102(a) as being anticipated by ss903337, September 1, 2000.

ss903337 teaches a sequence which includes a G/A polymorphism at the position corresponding to nucleotide 23 of SEQ ID NO: 73. A method of determining the position corresponding to position 23 of SEQ ID NO: 73, as well as a method which includes sequencing a region of the genomic DNA of a subject are considered inherent in the teachings of ss903337.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 2, 5, 7-10, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of ss903337 and Smith (Smith et al, Xenobiotica, vol. 28, pages 1129-1165, 1998).

ss903337 teaches a sequence which includes a G/A polymorphism at the position corresponding to nucleotide 23 of SEQ ID NO: 73. ss903337 does not provide a specific teaching of how this polymorphism in intron 3 of the CYP3A5 gene was detected, however Smith teaches that polymorphisms in genes encoding drug metabolizing enzymes, including the cytochrome P450 enzymes, can be detected by either a) amplification of a region of genomic DNA flanking the mutation site using PCR followed by the use of sequence specific restriction endonucleases, direct sequencing or SSCP to confirm the presence or absence of the mutation, b) use of allele specific PCR, or c) RFLP analysis followed by hybridization. Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use PCR followed by direct sequencing or hybridization to determine the identity of the nucleotide at the position corresponding to nucleotide 23 of SEQ ID NO: 73 in the CYP3A5 gene because Smith teaches that such are used to determine polymorphisms of drug metabolizing enzymes. In performing the method of ss903337 in view of Smith, the ordinary artisan would have been motivated to construct a number of different primers to amplify the polymorphic region. Such are considered equivalent to the claimed primers absent unexpected results.

13. Claims 6, and 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over ss903337 and Smith (Smith et al, Xenobiotica, vol. 28, pages 1129-1165, 1998), as applied to claims 1, 2, 5, 8-10, and 13-15 above, and further in view of Rootwelt (Rootwelt et al; Human Genetics, vol. 94, pp 235-239, 1994).

The method of ss903337 and Smith is set forth above. ss903337 and Smith do not teach using mismatch primers and restriction enzyme detection to determine the nucleotide sequence at

the position corresponding to nucleotide 23 of SEQ ID NO: 73, however Rootwelt teaches a method of detecting G/A mutations in a nucleic acid by using mismatch primers which introduce a Tru9I restriction site. Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use mismatch primers and restriction digestion using Tru9I in the method of ss903337 and Smith of determining the identity of a G/A polymorphism because Rootwelt teaches that it is an effective way to determine the identity of a G/A allele. The ordinary artisan would have been motivated to use the mismatch detection method of Rootwelt in the method of ss903337 and Smith for the purpose of developing an effective way identifying the G/A allele. Although ss903337 and Smith in view of Rootwelt does not teach using the specific mismatch primers set forth in the claims, motivated to construct a number of different primers to introduce the restriction site depending on the identity of the G/A allele. Such are considered equivalent to the claimed primers absent unexpected results.

14. Claims 8-9, 11, 13-15, and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Genbank Accession Number AC005020 (March 21, 2000) and Smith.

The claims have been broadly interpreted to encompass sequencing the CYP3A5 gene. Genbank Accession number AC005020 teaches the sequence of the CYP3A5 gene. Smith teaches that cytochrome P450 genes catalyse many important endogenous biochemical reactions and are involved in drug metabolism (see page 1129, pages 1152-1154). Smith also teaches that CYP3A is the major member of the CYP3A subfamily to be expressed in renal tissue (see page

1150). Smith teaches that inter-individual variation in P450 enzymes can have profound toxicological consequences, and that an accurate assessment of metabolic capacity can by made by DNA based genotyping assays in which the presence of specific DNA mutations can be detected (see page 1131, 2nd full para). Smith teaches that polymorphisms in genes encoding drug metabolizing enzymes, including the cytochrome P450 enzymes, can be detected by either a) amplification of a region of genomic DNA flanking the mutation site using PCR followed by the use of sequence specific restriction endonucleases, direct sequencing or SSCP to confirm the presence or absence of the mutation, b) use of allele specific PCR, or c) RFLP analysis followed by hybridization (see page 1131, lines 8-30). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to sequence the CYP3A5 gene for the purpose of analyzing the sequence to determine if any mutations are present that would be responsible for inter-individual variation in the CYP3A5 gene, as taught by Smith. The ordinary artisan would have been motivated to sequence and analyze the CYP3A5 gene to determine if any variation existed because Smith teaches that inter-individual P450 expression can have profound clinical consequences (page 1152) with regard to pharmacological responses to prescribed medications (page 1153, para 1), and that variation between individuals can influence disease susceptibility. In performing the method of AC005020 in view of Smith, the ordinary artisan would have been motivated to construct a number of primers pairs for the purpose of amplifying and sequencing the entire gene, which would include primers that are 5' and 3' to the positions set forth in the claims. With regard to claims 14-15 and 24-25, the claims are not directed to any specific sequence but are drawn to sequences and fragments of sequences "corresponding" to certain SEQ ID NOS which encompasses a large genus of possible primers.

The ordinary artisan, in performing the method of AC005020 and Smith would have been motivated to construct a number of different primers to amplify the CYP3A5 gene, including primers encompassed by the genus of primers in the instantly pending claims. Applicant can overcome this rejection for claims 14-15 and 24-25 by reciting instead "wherein primer X has the sequence of SEQ ID NO: [24, 26, 30, or 31] or a fragment thereof which is at least ten bases long, and primer Y has the sequence of SEQ ID NO: [25, 27, 16, or 32] or a fragment thereof which is at least ten bases long".

Conclusion

15. Claim 12 is allowable over the cited prior art.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jehanne Sitton
Primary Examiner
Art Unit 1634
5/26/05